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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

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Filing Date	02/04/2002
First Named	BIGGADIKE,
Group Art Unit	1616
Examiner Name	
Total Number of Pages in This Submission	
Attorney Docket Number	PG4734

ENCLOSURES *(check all that apply)*

- [ ] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment / Response
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [x] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
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- [ ] After Allowance Communication to Group
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- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) *(please identify below)*:

Remarks

GB0019172.6 filed August 05, 2000

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	James P. Riek Reg. No. 39,009
Signature	
Date	5 August 2002

23347
PATENT TRADEMARK OFFICE

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The Patent Office
Concept House
Cardiff Road
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South Wales
NP10 8QQ

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

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Dated 22 February 2002

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P01/7700 0.00-0019172.6

1/77

Patents Act 1977
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The Patent Office

Request for grant of a patent

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The Patent Office

Cardiff Road
Newport
Gwent NP9 1RH

1. Your Reference — MG/AJT/PG4153

2. Patent application number *(The Patent office will fill in this part)* — 05 AUG 2000 — 0019172.6

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

GLAXO GROUP LIMITED
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Patents ADP number *(if you know it)* 00473587003

If the applicant is a corporate body, give the country/state of its corporation

GB

4 Title of the invention — NOVEL COMPOUNDS

5 Name of your agent *(if you know one)*

ANDREW J. TEUTEN
(SEE CONTINUATION SHEET)

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

GLAXO WELLCOME PLC
GLAXO WELLCOME HOUSE, BERKELEY AVENUE
GREENFORD, MIDDLESEX
UB6 ONN, GB

Patents ADP number *(if you know it)* 07027683002

6. If you are declaring priority from one or more earlier patent applications, give the country and date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of Filing (day / month / year)

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing (day / month / year)

8. Is a statement of inventorship and of right to grant a patent required in support of this request? *(Answer yes if:*

a) any applicant named in part 3 is not an inventor, or

b) there is an inventor who is not named as an applicant, or

c) any named applicant is a corporate body.

See note (d))

YES

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Description	13
Claim(s)	4
Abstract	-
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10. If you are also filing any of the following, state how many against each item

Priority Documents	-
Translations of priority documents	-
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	-
Request for preliminary examination and search *(Patent Form 9/77)*	-
Request for substantive examination *(Patent Form 10/77)*	-
Any other documents *(please specify)*	-

11. **I/We request the grant of a patent on the basis of this application**

Signature Andrew J. TEUTEN Date 4 August, 2000

AGENT FOR THE APPLICANTS

12. Name and daytime telephone number of person to contact in the United Kingdom

Fiona Longstaff

020-8966 8234

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Patents Form 1/77

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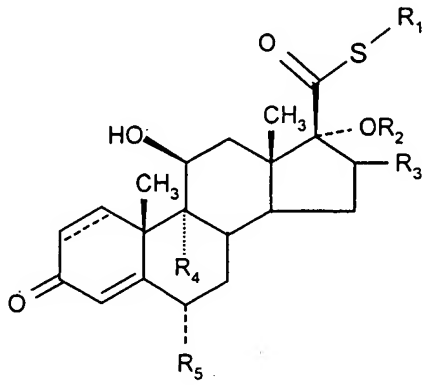
Novel Compounds

The present invention relates to novel anti-inflammatory and anti-allergic compounds of the androstane series and to processes for their preparation. The present invention also relates to pharmaceutical formulations containing the compounds and to therapeutic uses thereof, particularly for the treatment of inflammatory and allergic conditions.

Glucocorticosteroids which have anti-inflammatory properties are known and are widely used for the treatment of inflammatory disorders or diseases such as asthma and rhinitis. However, we have identified a novel series of glucocorticosteroids.

Thus, according to one aspect of the invention, there is provided a compound of formula (I)



(I)

wherein

R_1 represents C_{1-6} alkyl or C_{1-6} haloalkyl;

R_2 represents -C(=O)-aryl or -C(=O)-heteroaryl;

R_3 represents hydrogen, methyl (which may be in either the α or β configuration) or methylene;

R_4 and R_5 are the same or different and each represents hydrogen or halogen; and ⁼⁼⁼ represents a single or a double bond;

and salts and solvates thereof.

References to the term "aryl" include references to phenyl which may be optionally substituted with one or more substituents.

References to the term "heteroaryl" include references to 5 or 6 membered heterocyclic aromatic rings containing 1-3 hetero atoms selected from N, O and S (e.g. pyridinyl, pyrimidinyl, thiophenyl, furanyl, pyrrolyl, oxazolyl, thiadiazolyl) and preferably thiophenyl, pyrrolyl or furanyl, more preferably thiophenyl or furanyl, all of which may be optionally substituted with one or more substituents.

Examples of substituents for aryl and heteroaryl include C_{1-6} alkyl or halogen.

Examples of solvates include hydrates.

Examples of salts of compounds of formula (I) include physiologically acceptable salts which may be formed with basic compounds (such as when heteroaryl is basic) eg. acetate, benzoate, citrate, succinate, lactate, tartrate, fumarate and maleate.

References hereinafter to a compound according to the invention includes both compounds of formula (I) and salts and solvates thereof, particularly pharmaceutically acceptable salts and solvates.

It will be appreciated that the invention includes within its scope all stereoisomers of the compounds of formula (I) and mixtures thereof. Preferably, the absolute stereochemistry will be as shown in the representation of compounds of formula (I).

Examples of C_{1-6} haloalkyl that R_1 may represent include C_{1-6} alkyl substituted by 1-3 halogen atoms, preferably 1 halogen atom. Preferred halogen atoms are selected from bromine, chlorine and fluorine.

We prefer R_1 to represent fluoromethyl, chloromethyl, bromomethyl or 2'-fluoroethyl, especially fluoromethyl.

We prefer R_2 to represent –C(=O)-heteroaryl, preferably heteroaryl represents furanyl, pyrrolyl or thiophenyl, more preferably furanyl or thiophenyl eg. 2-furanyl, 3-furanyl, 2-thiophenyl or 3-thiophenyl, especially furanyl, particularly 2-furanyl.

We prefer R_3 to represent methyl, especially methyl in the α configuration.

Compounds of formula (I) in which R_4 and R_5, which can be the same or different, each represents hydrogen, fluorine or chlorine, particularly hydrogen or fluorine, are preferred. Especially preferred are compounds in which both R_4 and R_5 are fluorine.

A particularly preferred group of compounds of the present invention are compounds of formula (I) in which R_1 is fluoromethyl; R_2 is -C(=O)-2-furanyl; R_3 is methyl; R_4 and R_5, which can be the same or different, each represents hydrogen or fluorine, especially fluorine, and ⎓ represents a single or a double bond.

Preferably, ⎓ represents a double bond.

It is to be understood that the present invention covers all combinations of particularly and preferred groups referred to hereinabove.

Preferred compounds of formula (I) include:
6α,9α-Difluoro-17α-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester or a solvate thereof.

The compounds of formula (I) have potentially beneficial anti-inflammatory or anti-allergic effects, particularly upon topical administration, demonstrated by, for example, their ability to bind to the glucocorticoid receptor and to illicit a response via that receptor. Hence, the compounds of formula (I) are useful in the treatment of inflammatory and/or allergic disorders.

Examples of disease states in which the compounds of the invention have utility include skin diseases such as eczema, psoriasis, allergic dermatitis neurodermatitis, pruritis and hypersensitivity reactions; inflammatory conditions of the nose, throat or lungs such as asthma (including allergen-induced asthmatic reactions), rhinitis (including hayfever), nasal polyps, chronic obstructive pulmonary disease, interstitial lung disease, and fibrosis; inflammatory bowel conditions such as ulcerative colitis and Crohn's disease; and auto-immune diseases such as rheumatoid arthritis.

Compounds of the invention may also have use in the treatment of conjunctiva and conjunctivitis.

It will be appreciated by those skilled in the art that reference herein to treatment extends to prophylaxis as well as the treatment of established conditions.

As mentioned above, compounds of formula (I) are useful in human or veterinary medicine, in particular as anti-inflammatory and anti-allergic agents.

There is thus provided as a further aspect of the invention a compound of formula (I) or a physiologically acceptable salt or solvate thereof for use in human or veterinary medicine, particularly in the treatment of patients with inflammatory and/or allergic conditions.

According to another aspect of the invention, there is provided the use of a compound of formula (I) or physiologically acceptable salt or solvate thereof for the manufacture of a medicament for the treatment of patients with inflammatory and/or allergic conditions.

In a further or alternative aspect, there is provided a method for the treatment of a human or animal subject with an inflammatory and/or allergic condition, which method comprises administering to said human or animal subject an effective amount of a compound of formula (I) or physiologically acceptable salt or solvate thereof.

The compounds according to the invention may be formulated for administration in any convenient way, and the invention therefore also includes within its scope pharmaceutical compositions comprising a compound of formula (I) or physiologically acceptable salt or solvate thereof together, if desirable, in admixture with one or more physiologically acceptable diluents or carriers.

Further, there is provided a process for the preparation of such pharmaceutical compositions which comprises mixing the ingredients.

The compounds according to the invention may, for example, be formulated for oral, buccal, sublingual, parenteral, local or rectal administration, especially local administration.

Local administration as used herein, includes administration by insufflation and inhalation. Examples of various types of preparation for local administration include ointments, lotions, creams, gels, foams, preparations for delivery by transdermal patches, powders, sprays, aerosols, capsules or cartridges for use in an inhaler or insufflator or drops (e.g. eye or nose drops), solutions/suspensions for nebulisation, suppositories, pessaries, retention

enemas and chewable or suckable tablets or pellets (e.g. for the treatment of aphthous ulcers) or liposome or microencapsulation preparations.

Ointments, creams and gels, may, for example, be formulated with an aqueous or oily base with the addition of suitable thickening and/or gelling agent and/or solvents. Such bases may thus, for example, include water and/or an oil such as liquid paraffin or a vegetable oil such as arachis oil or castor oil, or a solvent such as polyethylene glycol. Thickening agents and gelling agents which may be used according to the nature of the base include soft paraffin, aluminium stearate, cetostearyl alcohol, polyethylene glycols, woolfat, beeswax, carboxypolymethylene and cellulose derivatives, and/or glyceryl monostearate and/or non-ionic emulsifying agents.

Lotions may be formulated with an aqueous or oily base and will in general also contain one or more emulsifying agents, stabilising agents, dispersing agents, suspending agents or thickening agents.

Powders for external application may be formed with the aid of any suitable powder base, for example, talc, lactose or starch. Drops may be formulated with an aqueous or non-aqueous base also comprising one or more dispersing agents, solubilising agents, suspending agents or preservatives.

Spray compositions may for example be formulated as aqueous solutions or suspensions or as aerosols delivered from pressurised packs, such as a metered dose inhaler, with the use of a suitable liquefied propellant. Aerosol compositions suitable for inhalation can be either a suspension or a solution and generally contain a compound of formula (I) and a suitable propellant such as a fluorocarbon or hydrogen-containing chlorofluorocarbon or mixtures thereof, particularly hydrofluoroalkanes, especially 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoro-n-propane or a mixture thereof. The aerosol composition may optionally contain additional formulation excipients well

known in the art such as surfactants e.g. oleic acid or lecithin and cosolvents e.g. ethanol.

Advantageously, the formulations of the invention may be buffered by the addition of suitable buffering agents.

Capsules and cartridges for use in an inhaler or insufflator, of for example gelatine, may be formulated containing a powder mix for inhalation of a compound of the invention and a suitable powder base such as lactose or starch. Each capsule or cartridge may generally contain between 20μg-10mg of the compound of formula (I). Alternatively, the compound of the invention may be presented without excipients such as lactose.

The proportion of the active compound of formula (I) in the local compositions according to the invention depends on the precise type of formulation to be prepared but will generally be within the range of from 0.001 to 10% by weight. Generally, however for most types of preparations advantageously the proportion used will be within the range of from 0.005 to 1% and preferably 0.01 to 0.5%. However, in powders for inhalation or insufflation the proportion used will be within the range of from 0.1 to 5%.

Aerosol formulations are preferably arranged so that each metered dose or "puff" of aerosol contains 20μg-2000μg, preferably about 20μg-500μg of a compound of formula (I). Administration may be once daily or several times daily, for example 2, 3, 4 or 8 times, giving for example 1, 2 or 3 doses each time. The overall daily dose with an aerosol will be within the range 100μg-10mg preferably, 200μg-2000μg. The overall daily dose and the metered dose delivered by capsules and cartridges in an inhaler or insufflator will generally be double those with aerosol formulations.

Topical preparations may be administered by one or more applications per day to the affected area; over skin areas occlusive dressings may

advantageously be used. Continuous or prolonged delivery may be achieved by an adhesive reservoir system.

For internal administration the compounds according to the invention may, for example, be formulated in conventional manner for oral, parenteral or rectal administration. Formulations for oral administration include syrups, elixirs, powders, granules, tablets and capsules which typically contain conventional excipients such as binding agents, fillers, lubricants, disintegrants, wetting agents, suspending agents, emulsifying agents, preservatives, buffer salts, flavouring, colouring and/or sweetening agents as appropriate. Dosage unit forms are, however, preferred as described below.

Preferred forms of preparation for internal administration are dosage unit forms i.e. tablets and capsules. Such dosage unit forms contain from 0.1mg to 20mg preferably from 2.5 to 10mg of the compounds of the invention.

The compounds according to the invention may in general may be given by internal administration in cases where systemic adreno-cortical therapy is indicated.

In general terms preparations, for internal administration may contain from 0.05 to 10% of the active ingredient dependent upon the type of preparation involved. The daily dose may vary from 0.1mg to 60mg, e.g. 5-30mg, dependent on the condition being treated, and the duration of treatment desired.

Slow release or enteric coated formulations may be advantageous, particularly for the treatment of inflammatory bowel disorders.

The pharmaceutical compositions according to the invention may also be used in combination with another therapeutically active agent, for example, a β_2 adrenoreceptor agonist, an anti-histamine or an anti-allergic. The invention

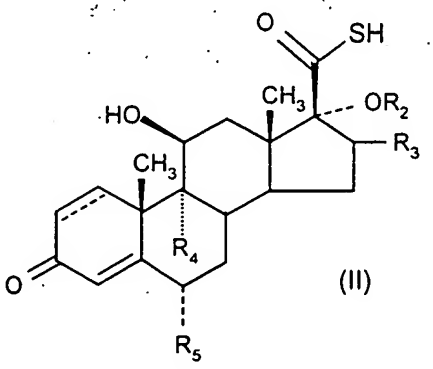
thus provides, in a further aspect, a combination comprising a compound of formula (I) or a physiologically acceptable salt or solvate thereof together with another therapeutically active agent, for example, a β_2-adrenoreceptor agonist, an anti-histamine or an anti-allergic.

The combination referred to above may conveniently be presented for use in the form of a pharmaceutical formulation and thus pharmaceutical formulations comprising a combination as defined above together with a pharmaceutically acceptable diluent or carrier represent a further aspect of the invention.

The individual compounds of such combinations may be administered either sequentially or simultaneously in separate or combined pharmaceutical formulations. Appropriate doses of known therapeutic agents will be readily appreciated by those skilled in the art.

The compounds of formula (I) and salts and solvates thereof may be prepared by the methodology described hereinafter, constituting a further aspect of this invention.

A process according to the invention for preparing a compound of formula (I) comprises alkylation of a thioacid of formula (II)



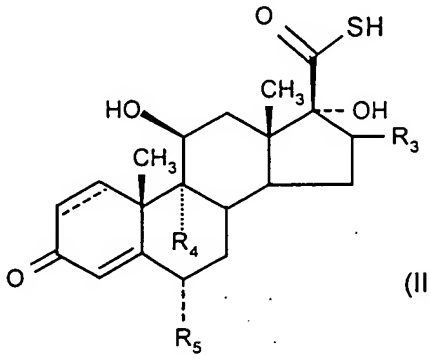
(II)

wherein R^2, R^3, R^4, R^5 and ⎓ are as defined above.

In this process the compound of formula (II) may be reacted with, for example, an appropriate alkyl or haloalkyl halide under standard conditions.

When R_1 represents fluoromethyl, the preferred haloalkyl halide reagent is bromofluoromethane.

Compounds of formula (II) may be prepared from the corresponding 17α-hydroxyl derivative of formula (III):



(III)

wherein R^2, R^3, R^4, R^5 and ⁼⁼⁼ are as defined above, using for example, the methodology described by G. H. Phillipps et al., (1994) Journal of Medicinal Chemistry, **37**, 3717-3729.

Compounds of formula (III) may be prepared in accordance with procedures described in GB 2088877B.

The following non-limiting Examples illustrate the invention:

EXAMPLES

General

Melting points were determined on a Kofler block and are uncorrected. ^{1}H-nmr spectra were recorded at 400 MHz and the chemical shifts are expressed in ppm relative to tetramethylsilane. The following abbreviations are used to describe the multiplicities of the signals: s (singlet), d (doublet), t (triplet), q

(quartet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets) and b (broad).

Intermediate 1: 6α, 9α-Difluoro-17α-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxo-androsta-1, 4-diene-17β-carbothioic acid

A solution of 6α, 9α-difluoro-11β, 17α-dihydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid (prepared in accordance with the procedure described in GB 2088877B) (18g, 43.64mmol) in anhydrous dichloromethane (200ml) and triethylamine (15.94ml, 114mmol) was treated at <5 °C with a solution of 2-furoyl chloride (11.24ml, 114mmol) in anhydrous dichloromethane (100ml) over approximately 40min. The solution was stirred at <5 °C for 30min. The resulting solid was collected by filtration, washed successively with 3.5% aqueous sodium hydrogen carbonate solution, water, 1M hydrochloric acid, and water and dried in vacuo at 60 °C to give a cream coloured solid. The dichloromethane filtrate was washed successively with 3.5% sodium hydrogen carbonate solution, water, 1M hydrochloric acid, water, dried (Na_2SO_4) and evaporated to give a cream coloured solid which was combined with that isolated above. The combined solids (26.9g) were suspended in acetone (450ml) and stirred. Diethylamine (16.8ml, 162mmol) was added and the mixture stirred at room temperature for 4.5h. The mixture was concentrated and the precipitate collected by filtration and washed with a little acetone. The washings and filtrate were combined, concentrated and loaded onto a silica gel Biotage column which was eluted with 24:1 chloroform: methanol. Fractions which contained the more polar component were combined and evaporated to give a cream coloured solid. This was combined with the solid isolated above and dried in vacuo to give a pale beige coloured solid (19.7g). This was dissolved in warm water, the pH adjusted to 2 with concentrated hydrochloric acid and the mixture extracted with ethyl acetate. The organic extract was dried (Na_2SO_4) and evaporated to give, after drying at 50°C, the title compound as a cream coloured solid (18.081g, 82%): LCMS retention time 3.88min, *m/z* 507 MH^+, NMR δ ($CDCl_3$) includes 7.61 (1H, m), 7.18 – 7.12 (2H, m), 6.52 (1H, dd, *J* 4, 2Hz), 6.46 (1H,

s), 6.41 (1H, dd, J 10, 2Hz), 5.47 and 5.35 (1H, 2m), 4.47 (1H, bd, *J* 9Hz), 3.37 (1H, m), 1.55 (3H, s), 1.21 (3H, s), 1.06 (3H, d, *J* 7Hz).

Example 1: 6α, 9α-Difluoro-17α-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester

A suspension of Intermediate 1 (2.5g, 4.94mmol) was dissolved in anhydrous N, N-dimethylformamide (25ml) and sodium hydrogen carbonate (465mg, 5.53mmol) was added. The mixture was stirred at –20°C and bromofluoromethane (0.77ml, 6.37mmol) was added and the mixture was stirred at –20°C for 2h. Diethylamine (2.57ml, 24.7mmole) was added and the mixture stirred at –20°C for 30min. The mixture was added to 2M hydrochloric acid (93ml) and stirred for 30min. Water (300ml) was added and the precipitate was collected by filtration, washed with water and dried in vacuo at 50°C to give a white solid which was recrystallised from acetone/water and dried in vacuo at 50°C to give the title compound (2.351g, 88%): LCMS retention time 3.66min, *m/z* 539 MH^+, NMR δ ($CDCl_3$) includes 7.60 (1H, m), 7.18 – 7.11 (2H, m), 6.52 (1H, dd, *J* 4.2Hz), 6.46 (1H, s), 6.41 (1H, dd, *J* 10, 2Hz), 5.95 and 5.82 (2H dd, *J* 51, 9Hz), 5.48 and 5.35 (1H, 2m), 4.48 (1H, m), 3.48 (1H, m), 1.55 (3H, s), 1.16 (3H, s), 1.06 (3H, d, *J* 7Hz).

Pharmacological Activity

Pharmacological activity was assessed in a functional in vitro assay of glucocorticoid agonist activity which is generally predictive of anti-inflammatory or anti-allergic activity in vivo.

The functional assay was based on that described by K.P.Ray et al., Biochem J. (1997), **328**, 707-715. A549 cells stably transfected with a reporter gene containing the NF-κB responsive elements from the ELAM gene promoter coupled to sPAP (secreted alkaline phosphatase) were treated with test compounds at appropriate doses for 1 hour at 37°C. The cells were then stimulated with tumour necrosis factor (TNF, 10ng/ml) for 16 hours, at which time the amount of alkaline phosphatase produced is measured by a

standard colourimetric assay. Dose response curves were constructed from which EC_{50} values were estimated.

In this test the compound in Example 1 showed an EC_{50} value of <1nM.

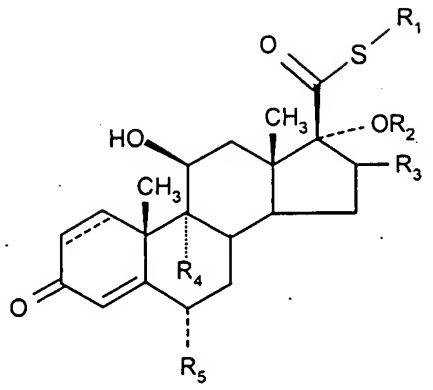
Throughout the specification and the claims which follow, unless the context requires otherwise, the word 'comprise', and variations such as 'comprises' and 'comprising', will be understood to imply the inclusion of a stated integer or step or group of integers but not to the exclusion of any other integer or step or group of integers or steps.

The application of which this description and claims forms part may be used as a basis for priority in respect of any subsequent application. The claims of such subsequent application may be directed to any feature or combination of features described herein. They may take the form of product, composition, process, or use claims and may include, by way of example and without limitation, the following claims.

The patents and patent applications described in this application are herein incorporated by reference.

CLAIMS

1. A compound of formula (I)



(I)

wherein

R_1 represents C_{1-6} alkyl or C_{1-6} haloalkyl;

R_2 represents -C(=O)-aryl or -C(=O)-heteroaryl;

R_3 represents hydrogen, methyl (which may be in either the α or β configuration) or methylene;

R_4 and R_5 are the same or different and each represents hydrogen or halogen; and

⎓ represents a single or a double bond;

and salts and solvates thereof.

2. A compound according to claim 1 in which R_1 represents fluoromethyl, chloromethyl, bromomethyl or 2'-fluoroethyl.

3. A compound according to claim 2 in which R_1 represents fluoromethyl.

4. A compound according to any one of claims 1 to 3 in which R_2 represents -C(=O)-heteroaryl.

5. A compound according to claim 4 in which R_2 represents -C(=O)-furanyl, pyrrolyl or thiophenyl.

6. A compound according to claim 5 in which R_2 represents -C(=O)-furanyl or thiophenyl.

7. A compound according to claim 6 in which R_2 represents -C(=O)-furanyl.

8. A compound according to claim 7 in which R_2 represents -C(=O)-2-furanyl.

9. A compound according to any one of claims 1 to 8 in which R_3 is methyl.

10. A compound according to any of claims 1 to 9 in which R_4 and R_5 are the same or different and each represents hydrogen, fluorine or chlorine.

11. A compound according to any one of claims 1 to 10 in which R_4 and R_5 are the same or different and each represents hydrogen or fluorine.

12. A compound according to any of claims 1 to 11 in which both R_4 and R_5 are fluorine.

13. A compound according to claim 1 in which R_1 is fluoromethyl; R_2 is -C(=O)-2-furanyl; R_3 is methyl; R_4 and R_5 are the same or different and each represents hydrogen or fluorine; and ----- represents a single or a double bond.

14. A compound according to claim 13 in which R_4 and R_5 are each fluorine.

15. A compound according to any one of claims 1 to 14 in which ----- represents a double bond.

16. A compound of formula (I) according to claim 1 which is 6α,9α-difluoro-17α-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester or a solvate thereof.

17. A compound of formula (I) as defined in any of claims 1 to 16 or a physiologically acceptable salt or solvate thereof for use in veterinary or human medicine.

18. Use of a compound of formula (I) as defined in any of claims 1 to 16 or a physiologically acceptable salt or solvate thereof for the manufacture of a medicament for the treatment of inflammatory and/or allergic conditions.

19. A pharmaceutical composition comprising a compound of formula (I) as defined in any of claims 1 to 16 or a physiologically acceptable salt or solvate thereof together, if desirable, in admixture with one or more physiologically acceptable diluents or carriers.

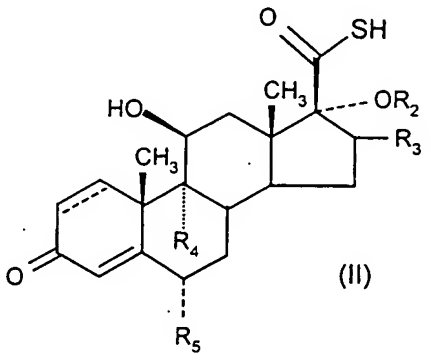
20. A pharmaceutical aerosol formulation comprising a compound of formula (I) as defined in any of claims 1 to 16 or a physiologically acceptable salt or solvate thereof, and a fluorocarbon or hydrogen-containing chlorofluoro carbon as propellant, optionally in combination with a surfactant and or a cosolvent.

21. A pharmaceutical composition according to claim 19 which further comprises another therapeutically active agent.

22. A pharmaceutical composition according to claim 21 in which said another therapeutically active agent is a β_2-adrenoreceptor agonist.

23. A method for the treatment of a human or animal subject with an anti-inflammatory and/or allergic condition, which method comprises administering to said human or animal subject an effective amount of a compound of formula (I) as defined in any of claims 1 to 16 or a physiologically acceptable salt or solvate thereof.

24. A process for preparing a compound of formula (I) according to claim 1 which comprises alkylation of a compound of formula (II)

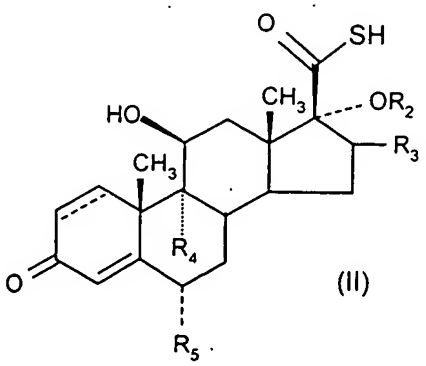


(II)

wherein R^2, R^3, R^4, R^5 and ═══ are as defined in claim 1.

25. A process according to claim 24 wherein alkylation is performed by reacting the compound of formula (II) with an appropriate alkyl or haloalkyl halide.

26. A compound of formula (II)



(II)

wherein R^2, R^3, R^4, R^5 and ═══ are as defined in claim 1.